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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,802	02/09/2005	Mathias Locher	42804-212835	6177

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EXAMINER	
BROOKS, KRISTIE LATRICE	
ART UNIT	PAPER NUMBER
1616	
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02/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,802	LOCHER ET AL.	
	Examiner	Art Unit	
	KRISTIE L. BROOKS	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 17-23 are pending.

2. Receipt and consideration of Applicants remarks filed October 13, 2009 is acknowledged.

3. Rejections not reiterated from the previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 17-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodfellow et al. (US Pub No. 2004/0214805) in view of Szelenyi et al., Loteprednol etabonate: A soft steroid for the treatment of allergic diseases of the airways, *Drugs of Today*, 36(5):313, 2000 (Abstract).

Applicant claims a method for the treatment of respiratory diseases, allergic diseases, asthma, and/or chronic obstructive pulmonary diseases comprising the step of administering loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide or a pharmaceutically acceptable salt thereof to a subject in need of treatment.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Goodfellow et al. teach treating pulmonary diseases such as chronic obstructive pulmonary disease or asthma by administered a phosphodiesterase-4 (PDE-4) inhibitor in combination with an anti-inflammatory corticosteroid (see the abstract). Examples of PDE-4 inhibitors include AWD-12-281 (i.e. N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide) (see page 3 paragraph 0027). The compounds may be administered together or separately (see page 1 paragraph 0008). The formulation may be administered as an inhalable preparation (e.g. liquid or powder) or orally (see page 3 paragraphs 0032-0034). Goodfellow et al. also teach a method of treating a pulmonary disease in a mammal comprising administering an

effective amount of a phosphodiesterase-4 (PDE-4) inhibitor in combination with an anti-inflammatory corticosteroid (see page 1 paragraph 0007).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Goodfellow et al. teach the combination of PDE-4 inhibitors and an anti-inflammatory but do not specifically teach loteprednol etabonate. This deficiency is cured by the teachings of Szelenyi et al.

Szelenyi et al. teach loteprednol etabonate as an antiallergic/antiasthmatic corticosteroid for the treatment of allergic diseases of the airways. It is highly suitable for nasal and pulmonary use (see the abstract).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

One of ordinary skill in the art would have been motivated to do incorporate loteprednol etabonate into the combination taught by Goodfellow et al. because Goodfellow et al. suggest the combination of PDE-4 inhibitors and anti-inflammatory corticosteroids. Further, loteprednol etabonate is known for use in the treatment of allergic and respiratory diseases as suggested by Szelenyi et al.

Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute loteprednol etabonate into the method taught

by Goodfellow et al. since it is an obvious variation of anti-inflammatory agents capable for use in the treatment of allergic and respiratory diseases taught by Goodfellow et al.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed composition.

Response to Arguments

Applicant's arguments filed October 13, 2009 have been fully considered but they are not persuasive.

Applicant argues that Goodfellow et al. do not teach loteprednol as a soft steroid and do not teach the synergistic inhibition of inflammation effect for any combination of a phosphodiesterase-4 inhibitor and an anti-inflammatory corticosteroid. Applicant also argues that Goodfellow et al. also argues that do not teach the unexpected and synergistic inhibition of inflammation when using the instantly claimed phosphodiesterase-4 inhibitor and an anti-inflammatory corticosteroid.

First, it should be noted that the features upon which applicant relies (i.e. synergy) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir.1993). Thus, Applicant's claims are drawn to administering loteprednol (a corticosteroid) and DFHO (

phosphodiesterase-4 inhibitor) in any amount for the treatment of respiratory and/or pulmonary diseases.

Goodfellow et al. teach treating pulmonary diseases by administering a combination of a phosphodiesterase-4 inhibitor (i.e. DFHO) and an anti-inflammatory corticosteroid. Thus, it is not a novel to treat pulmonary diseases by administering a combination of a phosphodiesterase-4 inhibitor and an anti-inflammatory corticosteroid. Goodfellow et al. do not teach loteprednol etabonate, but it is known in the art that loteprednol is a highly effective safe corticosteroid that is suitable for pulmonary use, as suggested by Szelenyi et al. Thus, it would have been obvious to incorporate loteprednol etabonate into the formulation taught by Goodfellow et al. because loteprednol is an obvious variation of corticosteroids that are useful in the treatment of pulmonary diseases.

Applicant argues that the instantly claimed combination of DFHO and loteprednol provide a synergistic inhibition of inflammation by inhibiting GS-CSF and TNF. The instant specification (see pages 6-9) discloses that the addition of 5nM DFHO lowered the IC_{50} value for loteprednol from 53.7nM to 13.4nM for the release and conversely, the addition of 10nM loteprednol to DFHO lowered the IC_{50} for DFHO from 3.2μM to 0.06μM. Thus, there is a superadditive effect brought about by the simultaneous administration of loteprednol and DFHO.

Applicant's data is not convincing. As mentioned above, Applicant is not claiming synergy. The instant claims are drawn to administering DFHO and loteprednol. There is no specific amount recited in the instant claims. Thus, one of ordinary skill in the art can

reasonably assume that loteprednol and DFHO can be administered any amount that will treat pulmonary diseases. Furthermore, Applicant has not provided data that compares the instant invention with the closest prior art (i.e. Goodfellow et al). It is already known in the art that the combination of a phosphodiesterase-4 inhibitor (i.e. DFHO) and an anti-inflammatory corticosteroid can be used to effectively treat pulmonary diseases, as suggested by Goodfellow et al. Applicant has not provided a side by side comparison with the closest prior art for one of ordinary skill in the art to establish whether any unexpected results have been demonstrated.

Therefore, Applicant' arguments are not convincing and the rejection is maintained.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616